



MEDICAL AND RESEARCH ADVISORY COMMITTEE (MARAC)

MARAC Statement: Temporary Suspension of Clinical Trials

March 1, 2021 - The Sickle Cell Disease Association of America's Medical and Research Advisory Committee (MARAC) is aware of the announcement on February 16, regarding the temporary suspension of bluebird bio clinical trials of **LentiGlobin Gene Therapy for Sickle Cell Disease** and the pause of all commercial use of bluebird bio European gene therapy.

Additionally, on February 22, the National Heart, Lung, and Blood Institute (NHLBI) temporarily suspended their unrelated gene therapy trial—**Pilot and Feasibility Study of Hematopoietic Stem Cell Gene Transfer for Sickle Cell Disease** at Boston Children's Hospital. The NHLBI stated that this temporary suspension was, "out of an abundance of caution" despite having no indications of harm.

On February 23, another gene therapy trial, **Gene Transfer for Patients with Sickle Cell Disease**, was also paused by the sponsor Aruvant.

MARAC has investigated the situation and met with bluebird bio to discuss the information available to the public. In the bluebird bio study, two patients developed blood cancer, and a third patient is under investigation for a related problem called myelodysplastic syndrome. The details of these patients are being examined by their doctors and the bluebird bio sponsors. Investigations are trying to determine whether the blood cancer can be linked to the gene therapy vector, the chemotherapy preparation for gene therapy, or damage of the host stem cell. No events occurred in the other clinical trials.

We value patient trust and patient concerns. SCDAA tries to express the voice of people living with sickle cell disease (SCD), and MARAC supports this mission with biomedical expertise. MARAC is monitoring developments and will continue to communicate findings to the SCD community. Nearly all the members of MARAC are involved in research to help those with SCD, and some who participated in developing this advisory statement are gene therapy investigators. The MARAC members with a potential conflict of interest due to their involvement in gene therapy clinical trials are listed on the following page.

MARAC acknowledges that there has been a history of clinical investigations that were unethical, including the infamous Tuskegee syphilis study, but this past week's events highlight that clinical research is no longer in that era. The modern safeguards for clinical research are working. Preplanned "stopping rules" triggered a "pause" of enrollment by bluebird bio when unusual and concerning events occurred. The Data Safety and Monitoring Board for the NHLBI gene therapy study followed "out of an abundance of caution," as did the Aruvant study. There were public announcements, and an intensive investigation is now underway to gather more information. The participants in the studies are being notified and are receiving appropriate medical care from the investigators.

Clinical research has been and continues to be the path for progress to improved SCD survival and quality of life. MARAC celebrates the decades of clinical research studies on which the progress in sickle cell care that we have today has been built — including penicillin, hydroxyurea, stroke screening and new medications.

SCDAA honors the SCD warriors who volunteer in clinical research. They have given their time so that others may benefit from new future treatments and cures. We pay tribute to all of those who have been lost to SCD, and we know many have died too young.

Dsiclosures:

Gene therapy study sponsor	Investigators	Other roles
bluebird bio	Julie Kanter, M.D. Raffaella Colombatti, M.D. Lakshmanan Krishnamurti, M.D.	Biree Andemariam, M.D., consultant Andrew Campbell, M.D., co-investigator, 2019 advisory board Baba Inusa, funded for ASCAT conference Elizabeth Klings, M.D., consultant on pulmonary function Sophie Lanzkron, M.D., chair of adjudication committee Kim Smith-Whitley, M.D., co-investigator Ahmar Zaidi, consultant/Honoraria
Aruvant		Biree Andemariam, M.D., consultant (past) Lewis Hsu, M.D., Data Safety Monitoring Board
NHLBI		Julie Kanter, M.D., protocol committee for BMTCTN-2001 Marsha Treadwell, Ph.D., consultant for Data Strategy Consortium
Vertex / CRISPR Therapeutics		Miguel R. Abboud, M.D., Data Safety Monitoring Board Biree Andemariam, M.D., consultant Kim Smith-Whitley, M.D., co-investigator

SCDAA Medical and Research Advisory Committee Members

Miguel R. Abboud, MD

Professor of Pediatrics and Pediatric Hematology-Oncology
Chairman
Department of Pediatrics and Adolescent Medicine
American University of Beirut, Lebanon

Shawn Bediako, PhD

Professor
Department of Psychology
University of Maryland Baltimore County
Baltimore, Maryland

Biree Andemariam, MD

Vice Chair, Sickle Cell Disease Association of America
Director, New England Sickle Cell Institute
Associate Professor of Medicine
University of Connecticut Health Farmington, Connecticut

Andrew Campbell, MD

Center for Cancer and Blood Disorders
Children’s National Health System
Associate Professor of Pediatrics
George Washington University School of Medicine and Health Sciences
Washington, DC

continued on next page

Raffaella Colombatti, MD, PhD

Physician Azienda Ospedaliera-Università di Padova
Department of Womens' and Child Health
Clinic of Pediatric Hematology Oncology
Via Giustiniani 3 35129
Padova, Italy

Lori Crosby, PsyD

Co-Director, Innovations in Community Research,
Division of Behavioral Medicine & Clinical Psychology
Co-Director, CCTST, Community Engagement Core
Psychologist, Research, Behavioral Medicine & Clinical
Psychologist
Cincinnati Children's
Professor, UC Department of Pediatrics
Cincinnati, Ohio

Deepika Darbari, MD

Center for Cancer and Blood Disorders
Children's National Health System
Professor of Pediatrics
George Washington University School of Medicine and
Health Sciences
Washington, DC

Payal Desai, MD

Associate Professor
Director of Sickle Cell Research
The Ohio State University
JamesCare at Ohio State East Hospital
Columbus, Ohio

James Eckman, MD

Professor Emeritus, Hematology & Medical Oncology
Emory University School of Medicine
Department of Hematology and Medical Oncology
Atlanta, Georgia

Mark Gladwin, MD

Professor and Chair
Department of Medicine
Founder, Pittsburgh Heart, Lung, and Blood Vascular
Medicine Institute
University of Pittsburgh
Pittsburgh, Pennsylvania

Jo Howard, MB Bchir, MRCP, FRCPath

Head of Red Cell/Sickle Cell Service
Guy's and St Thomas' NHS Foundation Trust
London, United Kingdom

Lewis Hsu, MD, PhD

Chair, Medical and Research Advisory Committee,
Sickle Cell Disease Association of America
Chief Medical Officer, Sickle Cell Disease
Association of America
Director of Pediatric Sickle Cell
Professor of Pediatric Hematology-Oncology
University of Illinois at Chicago
Chicago, Illinois

Baba Inusa

Professor of Paediatric Haematology
Lead Consultant Paediatric Sickle Cell and Thalassaemia
Evelina London Children's Hospital
Guy's and St Thomas' NHS Foundation Trust
Women and Children's Academic Health
Faculty of Life Sciences and Medicine
King's College
London, United Kingdom

Elizabeth Klings, MD

Associate Professor of Medicine
Director, Center for Excellence in Sickle Cell
Disease
Director, Pulmonary Hypertension Center
Boston University School of Medicine
Boston, Massachusetts

Lakshmanan Krishnamurti, MD

Professor of Pediatrics
Director of Bone Marrow Transplant
Joseph Kuechenmeister Aflac Field Force Chair
Aflac Cancer and Blood Disorders Center
Children's Healthcare of Atlanta/Emory University
Atlanta, Georgia

Sophie Lanzkron, MD

Director, Sickle Cell Center for Adults
The Johns Hopkins Hospital
Baltimore, Maryland

Julie Makani, FRCP, PhD

Associate Professor
Department of Haematology and Blood Transfusion
Muhimbili University of Health and Allied Sciences
Dar es Salaam, Tanzania

Caterina P. Minniti, MD

Director, Sickle Cell Center Montefiore Health System
Professor, Departments of Medicine and Pediatrics
Albert Einstein College of Medicine
Bronx, New York

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Genice T. Nelson, DNP, APRN, ANP-BC

Program Director, New England Sickle Cell Institute &
Connecticut Bleeding Disorders Programs,
UConn Health, Farmington, Connecticut
Board Member, Sickle Cell Disease Association of America

Isaac Odame, MB ChB, MRCP(UK), FRCPath, FRCPC, FRCPC

Professor, Department of Paediatrics
University of Toronto
The Hospital for Sick Children Division of Haematology/
Oncology
Toronto, Ontario

Kwaku Ohene-Frempong, MD

Director Emeritus, Comprehensive Sickle Cell Center
Emeritus Professor of Pediatrics, University of
Pennsylvania
President, Sickle Cell Foundation of Ghana
Emeritus Board Member, Sickle Cell Disease Association
of America

Gwendolyn Poles, DO

Former Medical Director, Kline Health Center
Faculty, Internal Medicine Program
UPMC Pinnacle
Harrisburg, Pennsylvania
Board Member, Sickle Cell Disease Association of America

John D. Roberts, MD

Yale Adult Sickle Cell Program
Smilow Cancer Hospital at Yale New Haven
New Haven, Connecticut

Wally Smith, MD

Professor
Scientific Director, VCU Center on Health
Disparities
Director, VCU Adult Sickle Cell Program
Department of Internal Medicine Division of General
Internal Medicine
Virginia Commonwealth University
Richmond, Virginia

Crawford J. Strunk MD

Director, Sickle Cell Disease and Hemoglobinopathy Clinic
Pediatric Hematology/Oncology Program
ProMedica Ebeid Children's Hospital
Toledo, Ohio

Immacolata Tartaglione, MD PhD

Department of Woman, Child and General and Specialist
Surgery
Università degli Studi della Campania "Luigi Vanvitelli"
Naples, Italy

Marsha Treadwell, PhD

Director, Sickle Cell Care Coordination Initiative
Regional Director, Pacific Sickle Cell Regional
Collaborative
Professor of Psychiatry and Pediatrics
University of California San Francisco Benioff Children's
Hospital Oakland
Oakland, California

Winfred C. Wang, MD

Emeritus, St. Jude Faculty
Member, Department of Hematology
St. Jude Children's Research Hospital
Memphis, Tennessee

Russell E. Ware, MD, PhD

Director, Division of Hematology
Co-Director, Cancer and Blood Diseases Institute
Director, Global Health Center
Marjory J. Johnson Chair of Hematology Translational
Research
Cincinnati Children's
Professor, UC Department of Pediatrics
Cincinnati, Ohio

Julie Kanter Washko, MD

Associate Professor, Division of Hematology Oncology
Director, Adult Sickle Cell Clinic
University of Alabama at Birmingham
Birmingham, Alabama

Kim Smith-Whitley, MD

Professor of Pediatrics
Director, Comprehensive Sickle Cell Center
Clinical Director, Division of Hematology
The Children's Hospital of Philadelphia
Philadelphia, Pennsylvania
Board Member, Sickle Cell Disease Association of America

Wanda Whitten-Shurney, MD

CEO & Medical Director
Sickle Cell Disease Association, Michigan Chapter Inc.
Detroit, Michigan
Board Member, Sickle Cell Disease Association of America

Ahmar U. Zaidi, MD

Assistant Professor of Pediatrics
Comprehensive Sickle Cell Center, Children's Hospital
of Michigan
Director of Physician Network Development, University
Pediatricians
Wayne State University/Central Michigan University School
of Medicine
Detroit, Michigan